UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,282	06/18/2001	Bonnie M Davis	U013469-7	6731

140 7590 07/08/2003

LADAS & PARRY
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER
JONES, DWAYNE C

ART UNIT	PAPER NUMBER
1614	9

DATE MAILED: 07/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,282	DAVIS, BONNIE M	
	Examiner	Art Unit	
	Dwayne C Jones	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-22,24-26 and 28-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7-22,24-26 and 28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Claims

1. Claims 1, 3-5, 7-22, 24-26, and 28-40.

2. Claims 1, 3-5, 7-22, 24-26, and 28-40.

3. Claims 2, 6, 23 and 27 were cancelled in the amendment of February 21, 2003.

Response to Arguments

4. Applicant's arguments filed February 21, 2003 have been fully considered but they are not persuasive. Applicant makes the following arguments. First, applicant argues that Shapiro et al. teach of treating many diseases with many compounds. Second, applicant alleges that Brossi et al. pertains to the making of phystigmine analogues. Third, applicant argues that there is no motivation to apply the delayed action of Conte et al. to treat Alzheimer's, which does not have diurnal variation.

5. Applicant first argues that Shapiro et al. teach of treating many diseases with many compounds. Independent claim 1 along with dependent claims 3-5, 7-19 are only directed to a pharmaceutical dosage containing a functionally description of a pharmaceutical agent, which happens to possess acetyl cholinesterase activity. Accordingly, the prior art reference of Shapiro et al. specifically teach the skilled artisan of a clinical treatment method for Alzheimer's disease with the administration of the acetyl cholinesterase inhibitor of galanthamine, (see column 30, lines 28-32 and column 32, lines 21 and 55-57). Moreover, Shapiro et al. is directed to the clinical treatment of

neurodegenerative diseases, which includes Alzheimer's disease, (see column 1, lines 22-29).

6. In addition, instant independent claim 1 recites the word "comprising", which is open-claim language. It is held that "the word 'comprising' incorporates additional steps of procedures and does not exclude materials or processes not recited in the claim". *Gould v. Mossinghoff, Comr. Pats.*, (DCCD 1982) 215 USPQ 310.

7. Second, applicant alleges that Brossi et al. pertains to the making of phystigmine analogues. However, instant claims 1, 3-5, 21, 22, 24-26 are only directed to the administration of an acetyl cholinesterase inhibitor. In addition, Brossi et al. teach that anticholinesterase inhibitors are useful in the treatment of Alzheimer's disease, (see column 1, lines 13-17). Brossi et al. teach of various pharmaceutical excipients, preparations and dosages of these acetyl cholinesterase inhibitors, (see columns 8-10).

8. Third, applicant argues that there is no motivation to apply the delayed action of Conte et al. to treat Alzheimer's, which does not have diurnal variation. It is first noted that it is the combination of the prior art references of Shapiro et al. in view of Conte et al. as well as the combination of Brossi et al. in view of Conte et al. that render the instant claims obvious rather than each of these references considered separately. Conte et al. provide the skilled artisan with the motivation that there is a need in the art for the rate-controlled delivery of medication, (see columns 1 and 2 on page 1017). Conte et al. also teach that "[i]t is well known that a drug must be given in the right dosage to produce the desirable effect, but the rate at which the active ingredient is administered/absorbed is also very important for its therapeutic effect." In addition,

Conte et al. disclose there is an increasing awareness that the drug must be administered not only in the right amount at a proper rate but also at the right time, (see column 1, page 1017). Conte et al. also disclose of a proper need in time-programmed release of drugs that are related to changes in the alternation between day and night (activity and rest). Conte et al. further state that there is a need to administer pharmaceuticals in forms that release the drug both at the best possible rate and at the best possible time. In fact, Conte et al. specifically teach the artisan of pharmaceuticals that, "are able to release a drug at a specific rate, but the release starts only after a well defined period of time, (as cited from column 2, page 1017). It could not be more clear from the teachings of Conte et al. that one having ordinary skill in the art is provided not only with the motivation but with explicit disclosures to make and prepare pharmaceuticals in a delayed-release or time-programmed release forms. Accordingly, the skilled artisan is provided with the necessary information to generate pharmaceuticals, such as those disclosed in Shapiro et al. and Brossi et al., for the treatment of Alzheimer's disease in a delayed-release or time-programmed release form as clearly taught by the prior art reference of Conte et al.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-5, 21, 22, 24-26, 39 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is insufficient descriptive support for the term/phrase a centrally acting acetyl cholinesterase inhibitor. In addition, the instant specification does not describe what is meant by the term/phrase a centrally acting acetyl cholinesterase inhibitor other than galanthamine, lycoramine, and rivastigmine. Structural identifying characteristics of the term/phrase a centrally acting acetyl cholinesterase inhibitor are not disclosed except for those galanthamine and lycoramine, and rivastigmine. There is no evidence that there is any per se structure/function relationship between the term/phrase a centrally acting acetyl cholinesterase inhibitor other than those disclosed, namely galanthamine and lycoramine, and rivastigmine. The instant specification does provide an adequate written description for the term/phrase of a centrally acting acetyl cholinesterase inhibitor. Accordingly, these claims fail to comply with the written description requirement.

11. Claims 21, 24-26 and 28-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is insufficient descriptive

support for the term/phrase a disease or condition in which it is desirable to administer a centrally –acting acetyl cholinesterase inhibitor. In addition, the instant specification does not describe what is meant by the term/phrase a disease or condition in which it is desirable to administer a centrally –acting acetyl cholinesterase inhibitor other than Alzheimer's disease. Structural identifying characteristics of the term/phrase a disease or condition in which it is desirable to administer a centrally –acting acetyl cholinesterase inhibitor are not disclosed except for those Alzheimer's disease. There is no evidence that there is any per se structure/function relationship between the term/phrase a disease or condition in which it is desirable to administer a centrally –acting acetyl cholinesterase inhibitor other than those disclosed, namely Alzheimer's disease. The instant specification does provide an adequate written description for the term/phrase of a disease or condition in which it is desirable to administer a centrally –acting acetyl cholinesterase inhibitor. Accordingly, these claims fail to comply with the written description requirement.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 3 and 4 depend on cancelled claim 2, which renders these claims vague and indefinite.

14. Claims 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. Claims 24 and 25 depend on cancelled claim 23, which renders these claims vague and indefinite.

Claim Rejections - 35 USC § 103

15. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

16. The rejection of claims 1, 3-5, 7-21, 22, 24-26, 28-38 under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al. in view of Conte et al. is maintained for both the reasons of above and of record. In addition, the rejection of Shapiro et al. in view of Conte is restated.

17. Shapiro et al. provide the necessary disclosure to the skilled artisan for a clinical treatment method of Alzheimer's disease with the administration of the acetyl cholinesterase inhibitor of galanthamine, (see column 30, lines 28-32 and column 32, lines 21 and 55-57). In addition, it would have been obvious to the skilled artisan to include or utilize other types of acetyl cholinesterase inhibitors, which would obviously embrace rivastigmine and lycoramine, in pharmaceutical preparations an also with the treatment of Alzheimer's disease. Moreover, Shapiro et al. is directed to the clinical treatment of neurodegenerative diseases, which includes Alzheimer's disease, (see column 1, lines 22-29).

18. The rejection of claims 1, 3-5, 21, 22, 24-26 under 35 U.S.C. 103(a) as being unpatentable over Brossi et al. in view of Conte et al. is maintained for both the reasons of above and of record. The rejection of Brossi et al. in view of Conte et al. will follow. First, the prior art reference of Brossi et al. pertains to the administration of acetyl

cholinesterase inhibitors. However, instant claims 1, 3-5, 21, 22, 24-26 are only directed to the administration of an acetyl cholinesterase inhibitor. In addition, Brossi et al. teach that anticholinesterase inhibitors are useful in the treatment of Alzheimer's disease, (see column 1, lines 13-17). Brossi et al. teach of various pharmaceutical excipients, preparations and dosages of these acetyl cholinesterase inhibitors, (see columns 8-10).

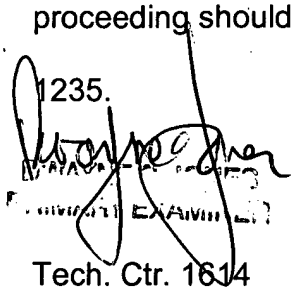
19. Next, the prior art references of Shapiro et al. and Brossi et al. are combined with Conte et al. in order to reject the instantly claimed invention. Conte et al. provide the skilled artisan with the motivation that there is a need in the art for the rate-controlled delivery of medication, (see columns 1 and 2 on page 1017). Conte et al. also teach that "[i]t is well known that a drug must be given in the right dosage to produce the desirable effect, but the rate at which the active ingredient is administered/absorbed is also very important for its therapeutic effect." In addition, Conte et al. disclose there is an increasing awareness that the drug must be administered not only in the right amount at a proper rate but also at the right time, (see column 1, page 1017). Conte et al. also disclose of a proper need in time-programmed release of drugs that are related to changes in the alternation between day and night (activity and rest). Conte et al. further state that there is a need to administer pharmaceuticals in forms that release the drug both at the best possible rate and at the best possible time. In fact, Conte et al. specifically teach the artisan of pharmaceuticals that, "are able to release a drug at a specific rate, but the release starts only after a well defined period of time, (as cited from column 2, page 1017). It could not be more clear

from the teachings of Conte et al. that one having ordinary skill in the art is provided not only with the motivation but with explicit disclosures to make and prepare pharmaceuticals in a delayed-release or time-programmed release forms. Accordingly, the skilled artisan is provided with the necessary information to generate pharmaceuticals, such as those disclosed in Shapiro et al. and Brossi et al., for the treatment of Alzheimer's disease in a delayed-release or time-programmed release form as clearly taught by the prior art reference of Conte et al. It would have been obvious to one having ordinary skill in the art to employ acetyl cholinesterase inhibitors, namely galanthamine, to treat Alzheimer's disease as taught by both Shapiro et al. and Brossi et al. Moreover, the skilled artisan is provided with the necessary motivation and teachings of Conte et al. to prepare pharmaceuticals in a delayed-release or time-programmed release forms, especially when the release of drugs at the best possible time that is related to changes in the alternation between day and night (activity and rest), as directly cited from Conte et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (703) 308-4634. The examiner can normally be reached on Mondays through Fridays from 8:30 am to 6:00 pm. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



Tech. Ctr. 1614
July 3, 2003